JUN 1 - 2005

6.0 510 (k) SUMMARY

SUBMITTED BY:

David M. Ikeda
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NAME OF DEVICE:

Trade Name: DiaSorin LIAISON® CMV IgG

Common Names/Descriptions: Immunoassay for the detection of IgG antibodies to human Cytomegalovirus (hCMV)

Classification Names: ENZYME LINKED IMMUNOABSORBENT ASSAY, CYTOMEGALOVIRUS

Product Code: LFZ

PREDICATE DEVICE: DiaSorin CMV IgG ELISA Kit (K955361)

DEVICE DESCRIPTION:

INTENDED USE: The LIAISON® CMV IgG assay uses chemiluminescent immunoassay (CLIA) technology on the LIAISON® Analyzer for the qualitative determination of IgG antibodies to human cytomegalovirus (hCMV) in human serum. It is intended to be used as an aid in the determination of serological status to CMV. LIAISON® Control CMV IgG kit is used in conjunction with LIAISON® CMV IgG immunoassay for monitoring substantial reagent failure.

KIT DESCRIPTION: The method for qualititative determination of specific IgG to hCMV is an indirect chemiluminescence immunoassay (CLIA). All assay steps (with the exception of magnetic particle resuspension) and incubations are performed by the LIAISON® Chemiluminescence Analyzer. The principal components of the test are magnetic particles (solid phase) coated with hCMV antigen and a conjugate of mouse monoclonal antibody to human IgG linked to an isoluminol derivative (isoluminol-antibody conjugate).
During the first incubation, hCMV antibodies present in the calibrators, samples or controls bind to the solid phase. During the second incubation, the antibody conjugate reacts with hCMV IgG already bound to the solid phase. After each incubation, the unbound material is removed with a wash cycle.
Subsequently, the starter reagents are added and a flash chemiluminescence reaction is thus induced. The light signal, and hence the amount of isoluminol-antibody conjugate, is measured by a photomultiplier as relative light units (RLU) and is indicative of the presence of hCMV IgG in calibrators, samples or controls.

PERFORMANCE DATA:

COMPARATIVE CLINICAL TRIALS: The clinical trials were conducted at two external US laboratories and at DiaSorin. Testing was performed on repository and prospective samples as defined below. The samples were tested by LIAISON® CMV IgG and comparison assay (DiaSorin CMV IgG ELISA Kit), at the trial sites per the manufacturers' instructions for use.

Prospective Samples: *Subjects Sent to Laboratory for CMV Testing:*

LIAISON® CMV IgG	CMV IgG ELISA			
	Negative	Equivocal	Positive	Total
Negative (<0.6 U/mL)	136	0	0	136
Equivocal (0.6-0.69 U/mL)	1	0	0	1
Positive (≥ 0.7 U/mL)	4	1	178	183
Total	141	1	178	320

	Percent Agreement		Exact 95% confidence interval
Positives	100.0%	(178/178)	97.95 - 100.0%
Negatives	96.45%	(136/141)	91.92 – 98.84%
Overall	98.13%	(314/320)	95.96 – 99.31%

Pregnancy Samples: *Subjects Sent to Laboratory for CMV Testing:*

LIAISON® CMV IgG	CMV IgG ELISA			
	Negative	Equivocal	Positive	Total
Negative (< 0.6 U/mL)	25	0	1	26
Equivocal (0.6-0.69 U/mL)	0	0	0	0
Positive (≥ 0.7 U/mL)	1	0	175	176
Total	26	0	176	202

	Percent Agreement		Exact 95% confidence interval
Positives	99.43%	(175/176)	96.88 - 99.99%
Negatives	96.15%	(25/26)	80.36 – 99.90%
Overall	99.01%	(200/202)	96.47 – 99.88%

Retrospective Samples: *Suspected Acute CMV Infection*

LIAISON® CMV IgG	CMV IgG ELISA			
	Negative	Equivocal	Positive	Total
Negative (< 0.6 U/mL)	0	0	0	0
Equivocal (0.6-0.69 U/mL)	0	0	0	0
Positive (≥ 0.7 U/mL)	0	0	100	100
Total	0	0	100	100

	Percent Agreement		Exact 95% confidence interval
Positives	100.0%	(100/100)	96.38 - 100.0%
Negatives	N/A		N/A
Overall	100.0%	(100/100)	96.38 - 100.0%

REPRODUCIBILITY: Reproducibility studies were performed at 4 sites using a coded panel comprised of 9 frozen repository serum samples. The serum panel was prepared to represent from low- to mid-positive analyte level. The same coded panel was tested at all sites, in three replicates per run for ten runs. Results expressed in U/mL are summarized in the following table.

ID#	N	mean (U/mL)	within run S.D.	within run %CV	between run S.D.	between run %CV	between site S.D.	between site %CV	overall S.D.	overall %CV
CGS1	90	0.91	0.04	4.84	0.11	9.39	0.06	6.55	0.11	12.29
CGS2	90	6.09	0.57	9.69	1.24	14.57	0.85	13.93	1.34	22.07
CGS3	90	1.59	0.10	6.05	0.14	8.21	0.07	4.60	0.16	10.31
CG1	90	1.15	0.04	3.76	0.12	5.36	0.12	10.35	0.12	10.88
CG2	90	0.94	0.04	3.95	0.09	6.01	0.08	8.13	0.09	9.86
CG3	90	0.84	0.04	5.01	0.09	7.24	0.08	9.41	0.10	11.46
CG4	90	0.68	0.02	3.60	0.05	5.34	0.05	6.76	0.06	8.43
CG5	90	0.68	0.03	4.63	0.06	5.12	0.06	8.47	0.07	9.88
CG6	90	1.17	0.07	6.02	0.06	5.17	0.03	2.20	0.09	7.68

INTERFERENCE: Controlled studies of potentially interfering substances showed that the assay performance was not affected by hemolysis (at 1000 mg/dL hemoglobin), lipemia (at 3000 mg/dL triglycerides), icterus (at 20 mg/dL bilirubin).

CROSS-REACTIVITY: The cross-reactivity studies for the LIAISON® CMV IgG assay were designed to evaluate potential interference from IgG immunoglobulins directed against closely-related members of the herpes virus family (EBV, HSV, VZV), from other organisms that may cause symptoms similar to CMV (Hepatitis A virus, Parvovirus B19) and from other conditions that may result from atypical immune system activity (ANA, rheumatoid factor).

Organism / condition	Number of Samples	Positive LIAISON® CMV IgG Result
EBV (VCA) IgG	25	(0/25)
HSV IgG	2	(0/2)
VZV IgG	1	(0/1)
Hepatitis A Ig	1	(0/1)
Parvovirus B19 IgG	11	(0/11)
ANA	3	(0/3)
RF	3	(0/3)
Total	46	(0/46)

None of the 46 total specimens tested from the disease panel was positive. There was no conclusive evidence of cross-reactivity observed, however due to the limited availability of certain samples, the possibility of cross-reactivity cannot be excluded.

WARNING: Assay interference due to circulating antibodies against HIV, Hepatitis A, Hepatitis B and Hepatitis C viruses has not been evaluated. The user is responsible for establishing cross-reactivity performance with these infectious agents.

CONCLUSION:
The LIAISON® CMV IgG assay showed equivalent performance to the corresponding FDA-cleared assay. The DiaSorin LIAISON® CMV IgG assay demonstrated agreement with the comparison method higher then 98% among prospectively collected routine samples, 99% among pregnancy samples and 100% agreement among retrospective selected samples. The results demonstrated that LIAISON® CMV IgG assay can be used with the LIAISON® Analyzer for the qualitative detection of IgG antibodies to hCMV and can be intended for use as an aid in the determination of serological status to CMV.

JUN 1 - 2005

6.0 510 (k) SUMMARY

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David M. Ikeda
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NAME OF DEVICE:

Trade Name: DiaSorin LIAISON® CMV IgM

Common Names/Descriptions: Immunoassay for the detection of IgM antibodies to human Cytomegalovirus (hCMV)

Classification Names: ENZYME LINKED IMMUNOABSORBENT ASSAY, CYTOMEGALOVIRUS

Product Code: LFZ

PREDICATE DEVICE: Diamedix Is-CMV IgM Capture ELISA Kit (K001767)

DEVICE DESCRIPTION:

INTENDED USE: The LIAISON® CMV IgM assay uses chemiluminescent immunoassay (CLIA) technology on the LIAISON® Analyzer for the qualitative determination of IgM antibodies to human cytomegalovirus (hCMV) in human serum. It is intended to be used as an aid in the diagnosis of acute CMV infection. LIAISON® Control CMV IgM kit is used in conjunction with LIAISON® CMV IgM immunoassay for monitoring substantial reagent failure.

KIT DESCRIPTION: The method for qualititative determination of specific IgM to hCMV is an indirect chemiluminescence immunoassay (CLIA). All assay steps (with the exception of magnetic particle resuspension) and incubations are performed by the LIAISON® Chemiluminescence Analyzer. The principal components of the test are magnetic particles (solid phase) coated with hCMV antigen, a buffer of goat IgG to human IgG and a conjugate of mouse monoclonal antibody to human IgM linked to an isoluminol derivative (isoluminol-antibody conjugate).
During the first incubation, calibrators, samples or controls are diluted with buffer A, which contains goat IgG to human IgG as an absorbent reagent to curb interference from human IgG specific to hCMV or from rheumatoid factor. During the second incubation, hCMV antibodies present in the calibrators, samples or controls bind to the solid phase. During the third incubation, the antibody conjugate reacts with hCMV IgM that is already bound to the solid phase. After each incubation, the unbound material is removed with a wash cycle.
Subsequently, the starter reagents are added and a flash chemiluminescence reaction is thus induced. The light signal, and hence the amount of isoluminol-antibody conjugate, is measured

by a photomultiplier as relative light units (RLU) and is indicative of the presence of hCMV IgM in calibrators, samples or controls.

PERFORMANCE DATA:

COMPARATIVE CLINICAL TRIALS: The clinical trials were conducted at two external US laboratories and at DiaSorin. Testing was performed on repository and prospective samples as defined below. The samples were tested by LIAISON® CMV IgM and comparison assay (Diamedix Is-CMV IgM Capture ELISA), at the trial sites per the manufacturers' instructions for use.

Prospective Samples: *Subjects Sent to Laboratory for CMV Testing (U.S. 610; European 889):*

LIAISON® CMV IgM	CMV IgM ELISA			
	Negative	Equivocal	Positive	Total
Negative (< 30 AU/mL)	1322	29	4	1355
Equivocal (30-34.9 AU/mL)	22	0	0	22
Positive (≥ 35 AU/mL)	74	9	39	122
Total	1418	38	43	1499

	Percent Agreement		Exact 95% confidence interval
Positives	90.70%	(39/43)	77.86 - 97.41%
Negatives	93.23%	(1322/1418)	91.80 – 94.48%
Overall	90.79%	(1361/1499)	89.22-92.21%

Pregnancy Samples: *Subjects Sent to Laboratory for CMV Testing:*

LIAISON® CMV IgM	CMV IgM ELISA			
	Negative	Equivocal	Positive	Total
Negative (< 30 AU/mL)	197	0	0	197
Equivocal (30-34.9 AU/mL)	1	0	0	1
Positive (≥ 35 AU/mL)	2	0	0	2
Total	200	0	0	200

	Percent Agreement		Exact 95% confidence interval
Positives	N/A		N/A
Negatives	98.50%	(197/200)	95.68 – 99.69%
Overall	98.50%	(197/200)	95.68 – 99.69%

Retrospective Samples: *Suspected Acute CMV Infection*

LIAISON® CMV IgM	CMV IgM ELISA			
	Negative	Equivocal	Positive	Total
Negative (< 30 AU/mL)	0	0	0	0
Equivocal (30-34.9 AU/mL)	0	0	0	0
Positive (≥ 35 AU/mL)	2	1	97	100
Total	2	1	97	100

	Percent Agreement		Exact 95% confidence interval
Positives	100.0%	(97/97)	96.27 - 100.0%
Negatives	0.0%	(0/2)	0 - 85.0%
Overall	97.0%	(97/100)	91.48 - 99.38%

REPRODUCIBILITY: Reproducibility studies were performed at 4 sites using a coded panel comprised of 9 frozen repository serum samples. The serum panel was prepared to represent from low- to mid-positive analyte level. The same coded panel was tested at all sites, in three replicates per run for ten runs. Results expressed in AU/mL are summarized in the following table.

ID#	N	mean (AU/mL)	within run S.D.	within run %CV	between run S.D.	between run %CV	between site S.D.	between site %CV	overall S.D.	overall %CV
CMS1	90	51.5	3.32	6.33	5.09	8.43	2.87	5.57	5.97	11.59
CMS2	90	117.6	5.77	4.87	12.43	7.59	9.05	7.70	13.33	11.34
CMS3*	90	<8.0	*110**	*4.62**	*247**	*4.89**	*260**	*10.77**	*265**	*10.97**
CM1	90	44.7	2.12	4.61	8.08	6.32	9.10	20.36	8.27	18.50
CM2	90	40.6	1.84	4.41	6.23	6.36	6.88	16.92	6.40	15.76
CM3	90	42.3	1.95	4.52	6.03	5.59	6.69	15.82	6.25	14.78
CM4	90	60.7	3.85	5.37	15.66	16.70	14.68	23.39	16.14	26.59
CM5	90	56.7	2.40	4.26	9.34	7.60	9.95	17.54	9.53	16.81
CM6	90	49.2	3.36	5.96	9.03	9.90	8.54	17.36	10.23	20.79

*The precision calculations for CMS3 are based on RLU data.

INTERFERENCE: Controlled studies of potentially interfering substances showed that the assay performance was not affected by hemolysis (at 1000 mg/dL hemoglobin), lipemia (at 3000 mg/dL triglycerides), icterus (at 20 mg/dL bilirubin).

CROSS-REACTIVITY: The cross-reactivity studies for the LIAISON® CMV IgM assay were designed to evaluate potential interference from IgM immunoglobulins directed against closely-related members of the herpes virus family (EBV, HSV, VZV, HHV6), from other organisms that may cause symptoms similar to CMV (Hepatitis A virus, Parvovirus B19) and from other conditions that may result from atypical immune system activity (ANA, rheumatoid factor).

Organism / condition	Number of Samples	Positive LIAISON® CMV IgM Result
EBV IgM	23	(0/23)
HSV IgM	2	(0/2)
VZV IgM	3	(0/3)
HHV6 IgM	2	(0/2)
Hepatitis A IgM	2	(0/2)
Parvovirus B19 IgM	17	(2/17)
ANA Ig	7	(0/7)
RF	11	(0/11)
Total	67	(2/67)

Two out of 67 total specimens tested from the disease panel were positive. Due to the limited availability of certain samples, the possibility of cross-reactivity cannot be excluded.

WARNING: Assay interference due to circulating antibodies against HIV, Hepatitis A, Hepatitis B and Hepatitis C viruses has not been evaluated. The user is responsible for establishing cross-reactivity performance with these infectious agents.

CONCLUSION:
The LIAISON® CMV IgM assay showed equivalent performance to the corresponding FDA-cleared assay. The DiaSorin LIAISON® CMV IgM assay demonstrated agreement with the comparison method higher then 90% among prospectively collected samples, 98% among pregnancy samples and 97% agreement among retrospective selected samples. The results demonstrate that LIAISON® CMV IgM assay can be used with the LIAISON® Analyzer for the qualitative detection of IgM antibodies to CMV and can be intended for use as an aid in the diagnosis of acute CMV infection.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

JUN 1 - 2005

David Ikeda
Manager, Regulatory Affairs & Quality Systems
DiaSorin Inc.
1951 Northwestern Ave.
P.O. Box 285
Stillwater, MN 55082

Re: k040290
Trade/Device Name: DiaSorin LIAISON® CMV IgG Assay
DiaSorin LIAISON® CMV IgM Assay
Regulation Number: 21 CFR 866.3175
Regulation Name: Cytomegalovirus serological reagents
Regulatory Class: Class II
Product Code: LFZ
Dated: May 24, 2005
Received: May 25, 2005

Dear Mr. Ikeda:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (240)276-0484. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html

Sincerely yours,

Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and
Radiological Health

Enclosure

Indications for Use

510(k) Number (if known): K040290

Device Name: LIAISON® CMV IgM

Indications For Use: The LIAISON® CMV IgM assay uses chemiluminescent immunoassay (CLIA) technology on the LIAISON® Analyzer for the qualitative determination of IgM antibodies to human cytomegalovirus (hCMV) in human serum. It is intended to be used as an aid in the diagnosis of acute CMV infection.

Prescription Use __X____ (Part 21 CFR 801 Subpart D) AND/OR Over-The-Counter Use _____ (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

510(k) K040290

Indications for Use

510(k) Number (if known): K040290

Device Name: LIAISON® CMV IgG

Indications For Use: The LIAISON® CMV IgG assay uses chemiluminescent immunoassay (CLIA) technology on the LIAISON® Analyzer for the qualitative determination of IgG antibodies to human cytomegalovirus (hCMV) in human serum. It is intended to be used as an aid in the determination of serological status to CMV.

Prescription Use __X____ (Part 21 CFR 801 Subpart D) AND/OR Over-The-Counter Use _____ (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

510(k) K040290